Remarks

Rejection of Claims 1-11 Under 35 U.S.C. § 112 ¶ 1

The Final Office Action maintained the rejection of claims 1-11 under 35 U.S.C. § 112 ¶ 1 as not enabled. Applicants respectfully traverse the rejection.

The basis for the rejection is that Applicants have not provided a nexus between an FPRL1 polypeptide and the recited diseases. Final Office Action at page 3, last paragraph. To advance prosecution, claims 1-11 have been amended to recite heart failure. Provided with the teachings of this specification, the skilled artisan would have perceived a nexus between the regulation of FPRL1 activity and heart failure.

At the priority date of this invention, the skilled artisan knew that stimulation of FPRL1 activates heterotrimeric G-proteins leading to an increase in intracellular calcium ion concentration. See Hu *et al.*, "Synthetic peptide MMK-1 is a highly specific chemotactic agonist for leukocyte FPRL1," *J. Leukocyte Biology 70*, 155-61, July 2001.[1] The increase in extracellular calcium ion concentration then triggers downstream cellular events. For cardiomyocytes, the cells of the heart atrium and ventricle, the cellular event triggered by an increase of intracellular calcium ions is contraction, which directly relates to cardiac function. Contracting cardiomyocytes pump blood at a rate commensurate with the requirements of the metabolizing tissue. Specification at page 55, lines 11-13. By modulating intracellular calcium ion concentrations in cardiomyocytes, for example by modulating FPRL1 activity, one could affect contraction of cardiomyocytes and thereby modulate the pumping force of the heart. Once provided with the specification's disclosure that FPRL1 mRNA is highly expressed in heart atrium and ventricle (see page 26, table 1, example 2), the skilled

[1] Provided with the accompanying IDS.

artisan can readily use the claimed screening methods to screen for therapeutic agents which regulate FPRL1 activity and which therefore could be used to treat heart failure. Identified inhibitors can be used to treat high-output heart failure, and identified activators can be used to treat low-output heart failure.

Rejection of Claims 1, 2, 4, 5, and 10 Under 35 U.S.C. § 102(b)

The Final Office Action maintains the rejection of claims 1, 2, 4, 5, and 10 as anticipated by Gronert[2] under § 102(b) of 35 U.S.C. Applicants respectfully traverse the rejection.

To determine whether a claim is anticipated by a prior art reference, one must first recognize each element of the invention recited in the claim and determine whether the prior art reference discloses the same element(s). *Kalman v. Kimberly-Clark Corp.*, 218 U.S.P.Q. 781, 789 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). Each of independent claims 1 and 2 recites a step which refers to heart failure, which Gronert plainly does not disclose. The Final Office Action does not disagree; however, it ignores these recited steps because Applicants allegedly have not provided an enabling disclosure. It is a fundamental rule of claim construction that every limitation is material and that what is claimed is what is defined by the claim as a whole. *General Foods Corp. v. Studiengesellschaft Kohle GmbH*, 972 F.2d 1272, 1280, 23 U.S.P.Q.2d 1839, 1345 (Fed. Cir. 1992). The Office is not free to ignore a recited element of the claim merely because it contends that step is not enabled.

Gronert does not anticipate claims 1, 2, 4, 5, and 10. Please withdraw the rejection.

[2] Gronert *et al.*, *J. Exp. Med. 187*, 1285-94, April 20, 1998.

Rejection of Claims 1-6 and 8-10 Under 35 U.S.C. § 103(a)

The Final Office Action maintains the three rejections under 35 U.S.C. § 103(a), each based on Gronert as the primary reference:

- claims 1-6 and 8-10 over Gronert in view of Fiore;[3]
- claim 7 over Gronert in view of Ramakrishnan;[4] and
- claims 1 and 11 over Gronert in view of Seo.[5]

The Office has not made a *prima facie* case of obviousness over Gronert in view of any of the cited references. A *prima facie* case of obviousness requires three elements:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

M.P.E.P., 8th ed., § 2142. Gronert does not disclose a connection between the recited polypeptide and heart failure, which is recited in each of independent claims 1 and 2. Gronert proposes a potential therapeutic benefit for LXA4 analogs.

None of the secondary references remedies this deficiency. Ramakrishnan discloses a G protein-coupled receptor related to FPRL1 which is not expressed in the heart. See the table on page 22.

[3] Fiore *et al.*, *J. Exp. Med. 180*, 253-60, 1994.

[4] Ramakrishnan, US 2002/0058259, filed March 14, 2001.

[5] Seo *et al.*, *J. Immunol. 158*, 1895-1901, 1997.

Seo discloses that FPRL1 is useful for activating microbicidal functions of human neutrophils. Page 1895, last line of the abstract. Seo does not teach or suggest a connection between FPRL1 and heart failure.

Fiore suggests that FPRL1 may be an LXA4 receptor in myeloid cells. Page 253, last line of the Summary. Fiore does not disclose expression of FPRL1 in the heart at all, much less specifically in the ventricle or atrium.

The disclosure that FPRL1 is highly expressed in the heart atrium and ventricle is found in the present specification, not in any of the cited combinations of references. There is nothing in any of the cited documents which would have motivated the person of ordinary skill to explore the usefulness of FPRL1 for screening for modulators useful in the treatment of heart failure.

The Final Office Action discounts the recitation in claims 1 and 2 of a disease which Gronert does not disclose because Applicants allegedly have not provided an enabling disclosure. Whether Applicants' disclosure is enabling irrelevant for determining whether any of the cited combinations of references renders the claimed methods obvious. The Office is not free to ignore a recited element of the pending claims. *General Foods Corp. v. Studiengesellschaft Kohle GmbH*, 972 F.2d at 1280, 23 U.S.P.Q.2d at 1345.

None of the cited combinations of references teaches or suggests the invention of the pending claims. Please withdraw the rejection.

Respectfully submitted,
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